It is noted that Applicants wish to obtain the benefit of foreign priority under 35 USC §119 (a)-(d) in reference to the priority application. Accordingly, Applicants enclose herewith an English translation of priority document Japanese Patent Application No. JP 10-32384/1998.

The specification was objected to on the grounds that the sequences for the M161Ag polynucleotide and polypeptide may not be incorporated by reference. It is believed that the amendments submitted herein obviate the rejection. In particular, Applicants enclose herewith a sequence listing for the M161Ag polynucleotide and polypeptide.

The Office Action also requested that a sentence appearing at page 1, 2nd paragraph (lines 6-8) of the specification be corrected. It is believed that the amendments submitted herein obviate the rejection. In particular, Applicants have deleted the objectionable term (See, e.g., the amendment to the specification set forth above. In particular, the term "almost" has been deleted from the noted sentence for purposes of clarification.

The specification is further objected to on the grounds that it does not contain a specific reference to the priority application. It is believed that the amendments submitted herein obviate the rejection. In particular, Applicants have inserted the requisite priority information into the application at page 1 just following the title of the application.

Reconsideration and withdrawal of each of the noted objections to the specification are thus requested.

Claims 9 and 10 were rejected under 35 USC §101, as allegedly being in improper form for process claims. It is believed that the amendments submitted herein obviate the rejection. In particular, Applicants have amended the noted claims accordingly to recite positive process steps.

Reconsideration and withdrawal of the rejections are thus requested.

Claims 1-10 were rejected under 35 USC §112, first paragraph, on the grounds that the sequence data for protein M161Ag was not adequately presented in the specification. As noted above, Applicants enclose herewith a sequence listing for the M161Ag polynucleotide and polypeptide, thus obviating the rejection.

Reconsideration and withdrawal of the rejection are thus requested.

Claims 1-2 and 6-10 stand rejected under 35 USC §112, first paragraph, as allegedly lacking enablement. As the rejection is understood, the Office Action acknowledges that the specification is enabling for cytokine inducers comprising a protein M161Ag, but that it is allegedly non-enabling for the remedy or therapeutic use of M161Ag for inducing a combination/group/list of the cytokines, namely IL-β, TNF-α, IL-6, IL-10, IL-12, and IFN-γ.

As the rejection is further understood, the position is taken that it would require "undue experimentation" to practice the scope of the invention claimed; e.g., to determine which cytokines are needed and have desirable biological activity in a particular therapeutic modality, and which cytokines should be considered as detrimental for therapy or remedy of the disease. The position also is taken that the specification allegedly does not provide adequate guidance as to what the outcome of such treatments would be in achieving an immunomodulatory response.

The rejection is traversed.

The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. In fact, there are many factors to be considered when

determining whether the specification is enabled and whether any necessary experimentation is "undue". They include: the breadth of the claims; the nature of the invention; the state of the prior art; the level of ordinary skill in the art; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention.

In view of thereof, Applicants respectfully submit that the scope of the claims is indeed enabled by the specification. In support of its argument concerning enablement, Applicants will submit under separate cover a copy of a recently published document entitled "Role of Toll-Like Receptors in Innate Immune Therapy for Cancer", together with an Information Disclosure Statement/PTO-1449 form so that the Examiner may properly consider the document's relevance. It is noted that such publication is pertinent to the therapeutic use of M161Ag.

Further, in rejecting claims 6-10 under 35 USC §112, first paragraph, the Office Action alleges that the specification does not reasonably provide enablement for the treatment or remedy of *all* immunological diseases. This rejection also is traversed and Applicants comments noted above concerning undue experimentation and the relevant factors to be considered are repeated.

It is respectfully submitted that the present application provides ample support and enablement to one skilled in the art, such that the full scope of the present invention could be practiced for the treatment of various immunological diseases. The most common examples include, but are not limited to, diseases such as cancer, allergies, autoimmune diseases, parasitic or latent microbism, sepsis and the like.

Thus, reconsideration and withdrawal of the rejection are requested.

Claims 1-2 and 9-10 stand rejected under 35 USC §112, second paragraph, on the basis of several alleged informalities.

Applicants respectfully submit that the noted claims have been amended in order to clarify or remove the noted informalities. Further, claims 9-10 have amended to recite positive process steps.

In view thereof, reconsideration and withdrawal of the rejections are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

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**VERSION MARKED TO SHOW CHANGES**

(Additions are underlined and deletions are bracketed in bold type.)

**IN THE SPECIFICATION**

Page 1, after the title of the invention, the following sentence has been added as a new/separate paragraph.

The present application is a continuation of PCT/JP99/00414, filed on February 1, 1999 which claimed the benefit of Japanese Patent Application No. JP 10-32384/1998, filed January 30, 1998.

Paragraph 2 appearing on page 1 has been replaced with the following rewritten paragraph:

M161Ag is a membrane protein which is contained in cells latently infected with *Mycoplasma fermentans* such as a human myelocytic leukemia cell line P39(+), and has functions such as activation of the alternative pathway and adsorption of the complement C3. Isolation and purification of this protein and preparation of monoclonal antibody have already been reported [Matsumoto et al., J. Exp. Med. 181, 115-125 (1995)]. Further, the primary structure has [almost] been reported [Nature Med., 3: 1266-1270 (1997)] (Japanese Patent Unexamined Publication No. Hei 9-157295).

The enclosed sequence listing has been inserted into the application between the last page of the specification (page 7) and the first page of the claims (page 8).

**IN THE CLAIMS**

The noted claims were amended as follows:

1. (amended) Cytokine inducers comprising a protein *Mycoplasma fermentans* 161 Ag (M161Ag) or gene recombination products thereof.

2. (amended) The cytokine inducers according to claim 1 wherein the induced cytokines are interleukin-1-beta (IL-1-β), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-10 (IL-10), interleukin-12 (IL-12) and/or interferon-gamma (IFN--γ) [INF-γ].

9. (amended) [Use of] A method of induction of cytokines comprising administration of protein M161Ag or gene recombination products thereof [for production of cytokine inducers].

10. (amended) [Use of] A method of treating immunological diseases comprising administration of protein M161Ag or gene recombination products thereof [for production of remedies for immunogical diseases].